

AMENDMENTS TO THE CLAIMS

1.-84. (Canceled)

85. (New) An isolated human antibody or functional fragment thereof that specifically binds an epitope of CD38 (SEQ ID NO: 22), wherein said antibody or functional fragment thereof mediates killing of a CD38+ target cell by antibody dependent cellular cytotoxicity with at least five-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the same or substantially the same conditions when a human PBMC cell is employed as the effector cell, wherein said CD38+ target cell is selected from the group consisting of LP-1 (DSMZ: ACC41) and RPMI-8226 (ATCC: CCL-155), and wherein the ratio of effector cells to target cells is between about 30:1 and about 50:1.
86. (New) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
87. (New) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
88. (New) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
89. (New) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
90. (New) An isolated functional fragment according to claim 85, which is a Fab or scFv antibody fragment.

91. (New) An isolated antibody to according to claim 85, which is an IgG.
92. (New) An isolated antibody to according to claim 91, which is an IgG1.
93. (New) An isolated human antibody or functional fragment thereof that specifically binds to an epitope of CD38 (SEQ ID NO: 22), wherein said antibody or functional fragment thereof mediates killing of a CD38-transfected CHO cell by cell dependent cytotoxicity with at least two-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the same or substantially the same conditions.
94. (New) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
95. (New) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
96. (New) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
97. (New) An isolated functional fragment according to claim 93, which is a Fab or scFv antibody fragment.
98. (New) An isolated antibody to according to claims 93, which is an IgG.
99. (New) An isolated antibody to according to claim 98, which is an IgG1.
100. (New) An isolated human or humanized antibody or functional fragment thereof comprising an antigen-binding region that competes for binding with an antibody which specifically binds to an epitope of CD38, wherein the epitope comprises an amino acid residue between 1 to 215 of CD38 (SEQ ID NO: 22).

101. (New) An isolated antibody or functional fragment thereof of claim 100, wherein the epitope comprises an amino acid residue found within amino acids 44-66, 82-94, 142-154, 148-164, 158-170, or 192-206 of CD38 (SEQ ID NO: 22).
102. (New) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
103. (New) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
104. (New) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
105. (New) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
106. (New) An isolated functional fragment according to claim 100, which is a Fab or scFv antibody fragment.
107. (New) An isolated antibody according to claim 100, which is an IgG.
108. (New) An isolated antibody according to claim 107, which is an IgG1.
109. (New) An isolated human antibody or functional fragment thereof that specifically binds to CD38, comprising a property selected from:
 - (a) an EC50 of less than or equal to 100 nM;
 - (b) antagonizes lymphocyte proliferation as well as chOKT10 antibody;
 - (c) antagonizes IL-6 release as well as chOKT10;

(d) mediates the killing of CD34+/CD38+ precursor cells by antibody dependent cellular cytotoxicity better than chOKT10; and
(e) is cross-reactive with cynomolgus CD38 and rhesus monkey CD38.

110. (New) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
111. (New) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
112. (New) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
113. (New) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
114. (New) An isolated functional fragment according to claim 109, which is a Fab or scFv antibody fragment.
115. (New) An isolated antibody according to claim 109, which is an IgG.
116. (New) An isolated antibody according to claim 115, which is an IgG1.
117. (New) A pharmaceutical composition comprising an antibody or functional fragment thereof according to claim 85 and a pharmaceutically acceptable carrier or excipient therefor.

118. (New) A method for treating a disorder or condition associated with the undesired presence of CD38+ cells, comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 117.
119. (New) A method according to claim 118, wherein said disorder or condition is a haematological disease.
120. (New) A method according to claim 118 selected from the group consisting of multiple myeloma, chronic lymphocytic leukemia, chronic myelogenous leukemia, acute myelogenous leukemia, and acute lymphocytic leukemia.
121. (New) A method according to claim 118, wherein said disorder or condition is an inflammatory disease.
122. (New) A method according to claim 121 selected from the group consisting of rheumatoid arthritis and systemic lupus erythematosus.
123. (New) An isolated epitope of CD38 consisting essentially of an amino acid sequence selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, 192-206 and 202-224 of CD38 (SEQ ID NO:22).
124. (New) The isolated epitope of CD38 according to claims 123, consisting of an amino acid sequence selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, 192-206 and 202-224 of CD38 (SEQ ID NO:22).
125. (New) A kit comprising (a) one or more isolated epitope(s) of CD38 according to claim 124;(b) an antibody library and (c) instructions for use.
126. (New) A variable heavy chain of an isolated antibody or functional fragment thereof that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 1, 2, 3, or 4, or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3, or 4, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.

127. (New) A variable light chain of an isolated antibody or functional fragment thereof that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 9, 10, 11, or 12, or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 9, 10, 11, or 12, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
128. (New) An isolated nucleic acid sequence that encodes an antigen-binding region of a human antibody or functional fragment thereof that is specific for an epitope of CD38.
129. (New) The nucleic acid sequence of claim 128, encoding a variable heavy chain of an isolated antibody or functional fragment thereof, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3 and 4 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3 or 4, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
130. (New) The nucleic acid sequence of claim 128, encoding a variable light chain of an isolated antibody or functional fragment thereof, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 9, 10, 11 and 12 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 9, 10, 11 or 12, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
131. (New) A vector comprising a nucleic acid sequence according to claim 128.
132. (New) An isolated cell comprising a vector according to claim 131.
133. (New) An isolated cell according to claim 135, wherein said cell is bacterial.
134. (New) An isolated cell according to claim 133, wherein said cell is mammalian.
135. (New) A method for targeting CD38+ cells in a subject or a cell sample, comprising the step of allowing said CD38+ cells to be contacted with an antibody or functional fragment thereof according to claim 1.

136. (New) A method of isolating a human or humanized antibody or functional fragment thereof comprising an antigen binding region which specifically binds to an epitope of CD38, comprising :
- a) contacting said epitope of CD38 with an antibody library; and
 - b) isolating said antibody or functional fragment thereof,
- wherein said epitope is a linear epitope.
137. (New) A method according to claim 136, wherein said linear epitope comprises amino acid residues 192-206 of CD38.
138. (New) A method of isolating a human or humanized antibody or functional fragment thereof comprising an antigen binding region which specifically binds to an epitope of CD38, comprising:
- a) contacting said epitope of CD38 with an antibody library; and
 - b) isolating said antibody or functional fragment thereof,
- wherein said epitope is a conformational epitope.
139. (New) A method according to claim 138, wherein said conformational epitope comprises one or more amino acid sequences selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, and 202-224 of CD38.
140. (New) An isolated antibody or functional fragment thereof according to claim 31, which comprises a heavy chain amino acid sequence selected from the group consisting of (i) SEQ ID NO: 6; and (ii) a sequence having at least 60 percent sequence identity in the CDR regions with the CDR regions depicted in SEQ ID NO: 6.
141. (New) An isolated antibody or functional fragment thereof according to claim 140, which comprises a light chain amino acid sequence selected from the group consisting of (i) SEQ ID NO: 14; and (ii) a sequence having at least 60 percent sequence identity in the CDR regions with the CDR regions depicted in SEQ ID NO: 14.